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A Systematic Review of Performance Ultrasound Diagnostic in Acute Cholecystitis

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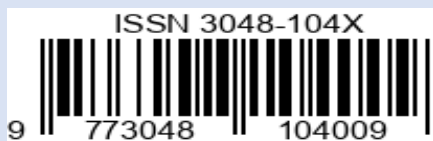
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ABSTRACT

Background: One of the most common causes of patients presenting to the emergency department with complaint of abdominal pain is acute cholecystitis. Acute cholecystitis, which is an inflammatory disease of the gallbladder, is mostly due to presence of a stone, ischemia, movement disorders in gallbladder and biliary tracts, and obstruction of the tracts by a tumor. **Methods:** This systematic review focused on full-text English literature published between 2014 and 2024 using the PRISMA 2020 guidelines. Editorials and review pieces published in the same journal as the submission without a DOI were not accepted. The literature was compiled using Medline, Science Direct, Scopus and Embase, among other online venues. **Result:** Five publications were found to be directly related to our ongoing systematic examination after a rigorous three-level screening approach. Subsequently, a comprehensive analysis of the complete text was conducted, and additional scrutiny was given to these articles. **Conclusion:** Diagnosing cholecystitis and appendicitis with ultrasound is more challenging for internist, surgeons and radiologists. We believe that ultrasound could be used as an adjunct to the clinical examination with the possibility to confirm but not exclude these diagnoses.

Keyword: Acute cholecystitis, diagnostic, imaging, ultrasound.

INTRODUCTION

Acute cholecystitis (AC) is a common disease that requires prompt and precise diagnosis to improve outcomes. According to Tokyo guidelines, no single physical exam finding or laboratory test carries sufficient weight to establish or exclude AC, and an imaging study should be used to confirm the diagnosis.^{1,2}

Acute cholecystitis (AC) affects 50-200 000 patients per year and accounts for 3-10% of patients who present to emergency departments (EDs) with complaints of abdominal pain. The Tokyo guidelines meta-analysis found that the incidence of acute cholecystitis in patients under 50 with abdominal pain is 6.3%, as compared to patients over 50, who are diagnosed with acute cholecystitis 20.9% of the time. Unsurprisingly, cholecystitis is the most common cause of abdominal pain in patients over 50.³ Common risk factors for cholecystitis include obesity, middle age, female gender, and pregnancy. Less common risk factors include active AIDS or *Ascaris lumbricoides* infection.³

Acute abdominal pain (AAP) is a common symptom for patients who visit the Emergency Department (ED) worldwide. Acute cholecystitis is one of the common causes of AAP. The incidence of acute cholecystitis was estimated at around 3–11% of the general population. Additionally, it is associated with a mortality rate of 0.8%. However, acute right upper quadrant (RUQ) pain has a wide range of differential diagnoses, including acute cholecystitis, acute cholangitis, liver abscess, and acute hepatitis. Hence, an accurate and

timely diagnosis of patients with acute RUQ pain is crucial.⁴

Diagnosis of acute cholecystitis must include all of the following information: history and physical examinations, laboratory results, and radiographic findings, such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). A validation study of the TG reported a sensitivity of 91.2% and specificity of 96.9%. However, approximately 28% of these patients were diagnosed with acute cholecystitis without fever and leukocytosis, especially in the elderly. Ultrasound is recommended for all suspected acute cholecystitis patients, since it is a simple and non-invasive procedure. Nevertheless, there are limitations because this score depends on the clinician's experience and expertise. The accuracy of the ultrasound alone has been debated, with a sensitivity ranging from 48% to 94%.^{4,5}

Ultrasound has long been the radiological investigation of choice for right upper quadrant pain for the detection of gallstones and cholecystitis. Although ultrasound has slightly reduced accuracy compared with cholescintigraphy, it has much greater clinical availability and familiarity. It is also superior to computed tomography, especially in the detection of gallstones and probably also in the detection of cholecystitis. Just how sensitive and specific ultrasound is in the detection of cholecystitis, as opposed to just gallstones, remains a question. Many previous studies have had low numbers of total patients examined, ranging from 26 to 186, or incomplete reporting of diagnostic metrics, or did not distinguish acute versus chronic

cholecystitis or include the latter in their study. Previous studies also used either exclusively fully trained consultants or attending radiologists or, in some cases, compared the performance of fully trained radiologists with that of either surgeon-performed or emergency department (ED) physician-performed ultrasound in the diagnosis of gallstones and cholecystitis.^{6,7}

METHODS

Protocol

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 standards were scrupulously followed by the work's author. The purpose of this was to make sure the study satisfied all the requirements. The chosen technique was carefully designed to ensure the accuracy and dependability of the investigation's findings.

Criteria for Eligibility

This study does a thorough evaluation of the last 10 years worth of literature on the correlation between body mass index genetic risk score and dietary intake on weight status. This study intends to improve and provide light on patient treatment procedures through a thorough examination of data. The primary goal of this paper is to highlight the significance of the noteworthy topics that have been identified across the literature.

To ensure the quality of the included information in this study, strict inclusion and exclusion criteria are applied. To be eligible for inclusion, papers must have been published in the English language between 2014 and 2024. Editorials, submissions without a DOI,

previously published reviews, and duplicate journal entries are some of the exclusion criteria.

Search Strategy

The keywords used for this research is "Performance ultrasound diagnostic in acute cholecystitis". The Boolean MeSH keywords inputted on databases for this research are: *("Cholecystitis"[MeSH Subheading] OR "Risk factor"[All Fields] OR "Prevalence" [All Fields]) AND ("Diagnosed"[All Fields] OR "Diagnostic"[All Fields]) AND ("Ultrasound"[All Fields]) OR ("Ultrasonography" [All Fields]))*

Data retrieval

The writers thoroughly evaluated the abstract and title of each manuscript before beginning this systematic review in order to assess each one's significance. Just articles that met the inclusion criteria and aligned with the article's objectives were selected for further examination. Ultimately, a definitive result was obtained from a consistent pattern found over several analyses. Only full-text, English-language submissions were acceptable. Content that satisfied all pre-established inclusion criteria and directly related to the study's subject matter was included after the most stringent screening procedure. Studies that failed to satisfy these requirements were frequently ignored, and their conclusions were not taken into consideration. A thorough analysis was conducted on a plethora of information discovered throughout the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.

Quality Assessment and Data Synthesis

The research that was reported in the titles and abstracts of each article was independently assessed by the authors in order to determine which papers needed additional investigation. Going over each document that satisfied the pre-established requirements to be included in the review was the following stage. The selection of an article for inclusion in the review was based on the evaluation procedure's results. By accelerating the selection of articles for further evaluation, this criterion was able to accomplish the goal of facilitating a thorough analysis of previous research and the factors that qualified them for the review.

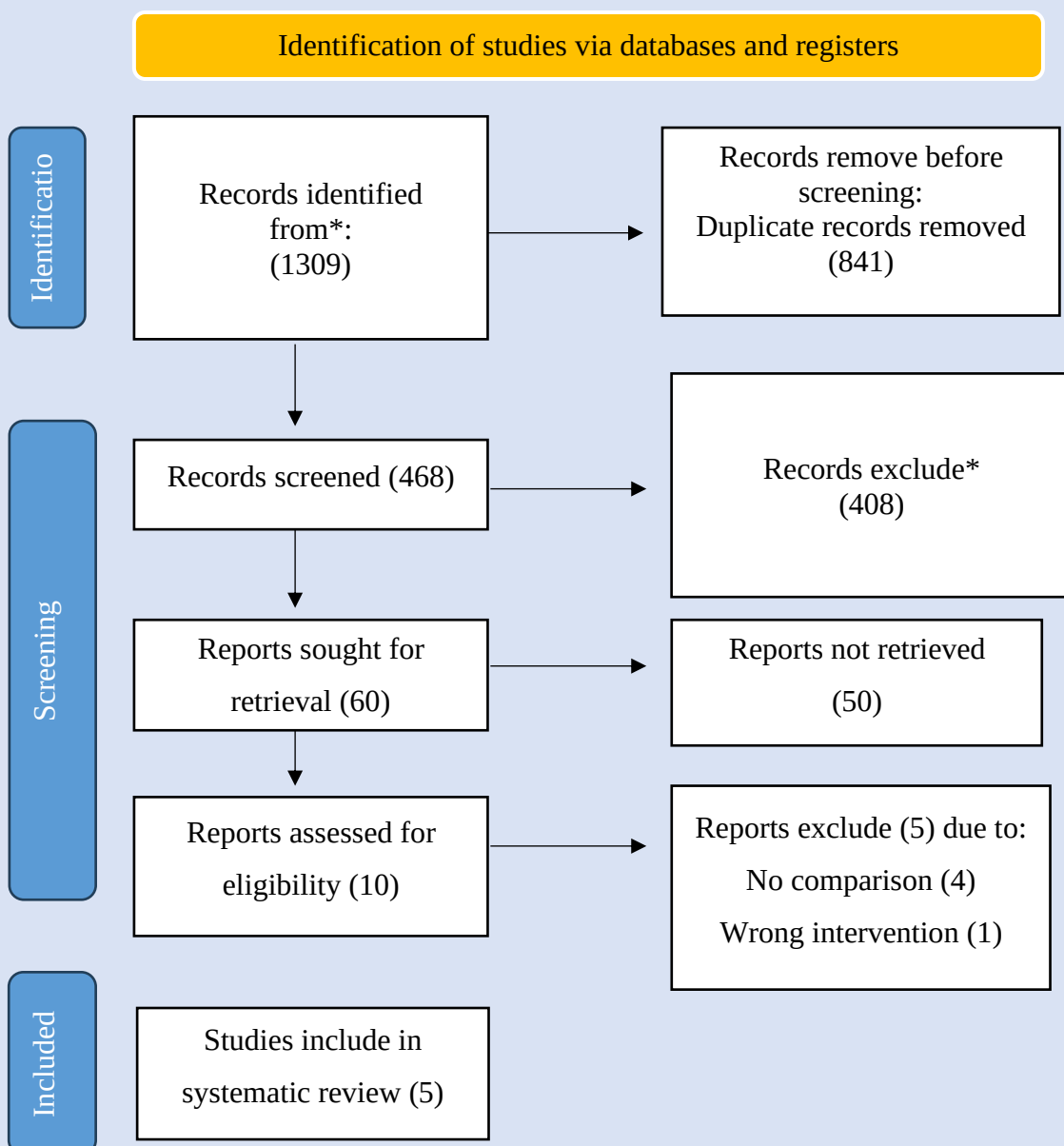


Figure 1. Article search flow chart

RESULT

Using reputable resources like Science Direct, PubMed, and SagePub, our research team first gathered 1309 publications. A thorough three-level screening strategy was used to identify only five papers as directly relevant to our ongoing systematic evaluation. Next, a thorough study of the entire text and further examination of these articles were selected. Table 1 compiles the literature that was analyzed for this analysis in order to make it easier to view.

Table 1. The literature included in this study

Author	Origin	Method	Sample Size	Result
Tourghabe, JV et al., 2018 ⁸	Iran	The present diagnostic accuracy study has been carried out on patients presenting to the emergency department with complaint of pain in the right upper quadrant of abdomen suspected with acute cholecystitis.	51	51 patients with the mean age of 42.3±15.8 (17-81) years were analyzed (82.4% female). The overall agreement between emergency medicine resident and radiologist in ultrasonographic diagnosis of cholecystitis was 0.421 (95% CI: 0.118-0.724). Based on the pathology and surgical findings, acute cholecystitis was confirmed for all 51 (100%) patients. Meanwhile, based on the ultrasonographic report of radiologist and emergency medicine resident only 45 (88.2%) and 34 (66.7%) patients, respectively, were diagnosed with cholecystitis. Screening performance characteristics of ultrasonography by radiologist for detection of gallbladder stone ($p = 0.010$) and gallbladder wall thickness ($p < 0.0001$) were significantly better than emergency medicine resident.

Perez, MG et al., 2021⁹	USA	In this IRB-approved and retrospective study, CAV was evaluated in 73 patients, 43 who underwent definitive treatment with cholecystectomy or percutaneous cholecystostomy and 30 control patients without clinical suspicion for cholecystitis.	73	Of the 43 patients who underwent definitive treatment, 25 had acute cholecystitis (34%) and 18 (25%) had chronic cholecystitis. Average CAV measurements were 50±16 cm/s (acute), 28±8 cm/s (chronic), and 22±8 cm/s (control; $p < 0.000$). In univariate analysis, among patients who underwent definitive therapy, $CAV \geq 40$ cm/s, gallbladder wall thickness, stone impaction, GB long dimension ≥ 8 cm, and elevated WBC were associated with acute cholecystitis ($p < 0.05$). In multivariate analysis, $CAV \geq 40$ cm/s was the only statistically significant variable ($p = 0.016$). $CAV \geq 40$ cm/s alone had a PPV of 94.7% and overall accuracy of 81.4% in diagnosing acute cholecystitis.
Evans, DP et al., 2021¹⁰	USA	We reviewed all ECUS performed between 2012 and 2017 that had a matching radiology performed ultrasound (RADUS) and a discharge diagnosis. 332 studies were	332	Using discharge diagnosis as the gold standard ECUS was 67% (56–78%) sensitive, 88% (84–92%) specific, NPV 90% (87–95%), PPV 60% (50–71%), +LR 5.6 (3.9–8.2), –LR 0.37 (0.27–0.52) for acute cholecystitis. RADUS was 76% (66–87%) sensitive, 97% (95–99%) specific, NPV 95% (92–97%), PPV 86% (76–95%), +LR 25.6 (12.8–51.4), and –LR 0.24 (0.15–0.38). ECUS was able to detect gallstones

		identified. The sensitivity and specificity of both ECUS and RADUS were compared to the patient's discharge diagnosis.		with 93% (89–96%) sensitivity and 94% (90–98%) specificity leading to a NPV 90% (85–95%), PPV of 95% (92–98%), +LR 14.5 (7.7–27.4), –LR 0.08 (0.05–0.13). The unweighted kappa between ECUS and RADUS was 0.57. The median time between obtaining ECUS vs. RADUS diagnosis was 124 min.
Wertz, JR et al., 2018 ¹¹	Mexico	AC was diagnosed in 60 patients (62 patient encounters) between July 1, 2013, and July 1, 2015. Of these patients, 56 underwent US, 48 underwent CT, and 42 underwent both.	60	The sensitivity of CT for detecting AC was significantly greater than that of US: 85% versus 68% ($p = 0.043$), respectively; however, the negative predictive values of CT and US did not differ significantly: 90% versus 77% ($p = 0.24–0.26$). Because there were no false-positives, the specificity and positive predictive values for both modalities were 100%. Among the 42 patients who underwent CT and US, both modalities were positive for AC in 25 patients, CT was positive and US was negative in 10 patients, and US was positive and CT was negative in two patients; in five patients, both US and CT were negative.
Naidu, K et al., 2016 ¹²	Australia	A 5-year retrospective analysis equal to the TG 2013 validation process of all	169	Inclusion criteria were met by 169 patients with a prevalence of acute cholecystitis of 52.7 %. The individual features of fever, gallbladder wall thickening and probe

		emergency cholecystectomies for acute cholecystitis or persistent biliary pain with an ultrasound performed during the same admission. Acute cholecystitis at histology was the golden standard.		tenderness were not significant in univariate analysis. In multivariate analysis only, neutrophil count was an independent predictor. The combined application of the TG 2013 guidelines led to a better sensitivity of 83.1 % at the cost a reduced specificity of 37.5 % compared to neutrophil count alone. The accuracy was therefore only 60.3 %, which was well below the TG 2013 report.
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Tourghabe, JV et al., 2018⁸ showed relying solely on ultrasonography for making a decision regarding surgery of patients with pain in the right upper quadrant of their abdomen suspected with cholecystitis is not accurate enough. However, the screening performance characteristics of ultrasonography by radiologist in detection of gallstones and increased thickness of gallbladder wall were significantly better.

Perez, MG et al., 2021⁹ showed elevated peak systolic cystic artery velocity is an objective imaging biomarker that may help improve accuracy of abdominal ultrasound in diagnosis of acute cholecystitis in patients presenting to the ED with right upper quadrant abdominal pain.

Evans, DP et al., 2021¹⁰ showed ECUS is a valuable screening tool in the hands of the emergency physician, which can improve time to diagnosis and potential disposition, in patients in whom biliary colic is suspected. ECUS also has the potential to decrease time to intervention when there is high clinical suspicion of acute cholecystitis. If ECUS is equivocal for a patient in whom the emergency physician has suspicion for biliary pathology, then a confirmatory RADUS should be obtained.

Wertz, JR et al., 2018¹¹ showed the sensitivity of US (68%) and CT (85%) for AC were not as good as sensitivities reported in prior studies: 81% for US and 94% for CT. CT at our institution was statistically significantly better for the diagnosis of AC than US, most likely because of an unclear clinical picture, the patient population, and a high proportion of poor-quality US examinations. However, US is still our first test of choice if AC is suspected clinically,

whereas CT is performed when the clinical picture is unclear. US and CT are complementary: If the initial test is negative and there is clinical suspicion of AC or if the initial examination is equivocal, the other examination should be performed. In our practice if both studies are negative for AC and clinical suspicion is high for AC, hepatiminodiacetic acid scanning is performed.

Naidu, K et al., 2016¹² showed neutrophil count to be the only independent predictor of acute cholecystitis, although its predictive values were not satisfactory. Ultrasound findings did not make an independent contribution in the diagnosis of acute cholecystitis. The application of the 2013 Tokyo Guidelines as a whole did lead to a slightly better identification of patients with acute cholecystitis, but also led to the over diagnoses of nearly two-thirds of the patients with chronic cholecystitis or normal gallbladders leaving a mediocre overall accuracy of only 60.3 %.

DISCUSSION

Acute cholecystitis is an acute inflammatory condition of the gallbladder; 95% of cases of acute cholecystitis are due to an obstructing calculus in the gallbladder neck or cystic duct. Obstruction of the cystic duct results in an overdistension of the gallbladder and a rise in intraluminal pressure. This increased pressure, along with cholesterol-supersaturated bile, triggers an acute inflammatory response. Gallstones contribute to the inflammatory response by stimulating prostaglandins I₂ and E₂. Secondary bacterial infection is present in 20% of cases of acute cholecystitis. Mural ischaemia resulting from the

increased intraluminal pressure may also contribute to complications such as gangrenous cholecystitis and perforation. Pathologically, there are three stages of inflammatory disease: (a) oedematous cholecystitis; (b) necrotising cholecystitis; and (c) suppurative cholecystitis.^{13,14}

The most common etiology of cholecystitis is cholelithiasis, with 90-95% of acute cholecystitis cases having gallstones. The remaining 5-10% of cases are acalculous. Furthermore, approximately 12% of patients with who are diagnosed with cholelithiasis will go on to develop acute cholecystitis within the next 5-7 years.³

Clinical symptoms and signs of AC had varying sensitivity and specificity. The Tokyo guidelines suggest using imaging studies such as US, CT, and HIDA scans for the diagnosis of AC, in conjunction with detailed history, complete clinical examination, and laboratory tests. Although HIDA has excellent diagnostic performance for AC with a sensitivity and specificity above 90%, its utilization is limited in emergency practice due to the required resources, time, and exposure to radioactive isotopes. By contrast, US is a valuable tool for its non-ionizing, low-cost, and easy-to-use characteristics. US is considered the first-line imaging modality in recently published guidelines for the diagnosis of AC. Our review provides the evidence that US is a good diagnostic tool with discriminative power.¹⁵

The use of ultrasound (US) outside the radiology department, often referred to as point-of-care ultrasound (POCUS), has increased in the last decades as more compact and portable scanners have become

available. At Stockholm South General Hospital's surgery department, abdominal POCUS has been part of surgical resident training since 2004. We have previously shown that surgeon-performed ultrasound (SPUS) at the emergency department (ED) results in fewer additional examinations, fewer admissions and shorter lead times to surgery.^{16,17}

Diagnostic imaging modalities for AC include ultrasound (US), computed tomography (CT), or hepatobiliary iminodiacetic acid (HIDA) scan. A 2012 meta-analysis reported that the HIDA scan had the highest diagnostic accuracy for A. However, US has non-radiating, easily accessible, and inexpensive characteristics, becoming the first-line diagnostic tool in emergency settings. In recent years, there has been a significant increase in the number of publications regarding the use of US for the diagnosis of AC. Up-to-date evidence is still lacking. Further, US is performed by radiologists traditionally. It is unclear whether the diagnostic performance differs when performed by other sonographers such as emergency physicians (EPs) or surgeons.¹⁵

Due to the wide availability of computed tomography (CT) scanners in emergency departments, increasing numbers of patients undergo CT examinations for suspected acute cholecystitis. Ultrasonography (US) remains the preferred initial imaging modality for the evaluation of suspected acute calculous cholecystitis due to its relatively low cost, easy accessibility, short examination duration and lack of ionising radiation. The distinct advantages of US over other imaging techniques are its high sensitivity and

specificity in detecting gallstones, and its ability to elicit 'Murphy's sign' using the ultrasound transducer. However, US has limited value in the evaluation of underlying complications of acute cholecystitis. Evaluation of such complications may require cross-sectional imaging techniques, namely CT or magnetic resonance (MR) imaging, for accurate localisation and surgical planning. CT and MR imaging can also be used to evaluate or exclude other pathologies that can present with right upper quadrant pain.¹³

CONCLUSION

Diagnosing cholecystitis and appendicitis with ultrasound is more challenging for internist, surgeons and radiologists. We believe that ultrasound could be used as an adjunct to the clinical examination with the possibility to confirm but not exclude these diagnoses.

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